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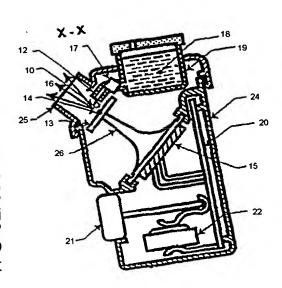
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(54) Title: METHOD AND DEVICE FOR ULTRASOUND DRUG DELIVERY



(57) Abstract: The present invention concerns a device for creating a directed spray of liquid or powder particles which is produced by contacting the liquid or powder with a radiation surface of an ultrasonic transducer such as a piezofilm or ultrasound tip. The ultrasonic waves cause the spray to project outwardly from the radiation surface and directs it into a patient's mouth or onto another target. Directed particle spray delivers sharp dosage and uniformed up to 90 % particle size drug delivery.

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METHOD AND DEVICE FOR ULTRASOUND DRUG DELIVERY

FIELD OF THE INVENTION

The present invention relates to a drug delivery system. In particular the present invention relates to a pocket size or hand held ultrasonic-pulmonary drug delivery system.

BACKGROUND OF THE INVENTION

In many medical applications it is necessary to make aerosols from liquids and powders. One of the therapeutic medical uses of ultrasound waves is in liquid aerosol mist production. Aerosol mist production makes use of a nebulizer or inhaler to produce an aerosol mist for creating a humid environment and delivering a drug to the lung.

Particularly for oral-pulmonary applications it is necessary to atomize medications, such as antibiotics, insulin, asthma drugs, and other drugs to make an aerosol that reaches the mouth, boucle, intestine and consequently the lungs.

Ultrasonic nebulizers operate by passing ultrasound waves of sufficient intensity through a liquid, the waves being directed at an air-liquid interface of the liquid from a point underneath or within the liquid. Liquid particles are ejected from the surface of the liquid into the surrounding air following the disintegration of capillary waves produced by the ultrasound. This technique can produce a very fine dense fog or mist. Aerosol mists produced by ultrasound are preferred because a smaller particle size of the aerosol can be obtained with the ultrasonic waves.

One of the major shortcomings of known ultrasonic inhalers and nebulizers is that there is no directed aerosol to the target. Therefore, an air stream is required to direct the aerosol to the target; however, this decreases the efficiency of ultrasound mist.

The device of the present invention comprises a means for creating a directed spray of liquid or powder particles produced by contact of the liquid or powder with a radiation surface of any ultrasound transducer such as, for example, a piezofilm or ultrasound tip. The ultrasonic waves cause the spray to project outwardly from the radiation surface of the transducer, and a particle spray is directed to the mouth.

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Accordingly, the device of the present invention generates a directed particle spray, created by ultrasound waves, into a mouth and delivers sharp dosage of a uniform up to 90 % particle size drug.

Furthermore, the ultrasound waves used in the device energize the drug and cause penetration of the drug below the surface of the tissue.

Finally, the device of the present invention for drug delivery is particularly advantageous when sharp dosage drug delivery is desirable, such as, for example, with insulin for diabetic care. Piezoelectric oscillatory and liquid atomization system, is known with a bending oscillator or working plate for atomization of liquid. A disadvantage of the these piezoelectric atomizers is that the particle sizes are not uniform and particle sizes of about 0.1 micron to several millimeters are obtained. The particles of larger diameter must be retained by means of a mechanical droplet separator.

A number of prior art references are available in the art, each of which references are directed to some specific discreet elements of the system which is described and claimed in the present invention, however, none of which is directed to the totality of the combination, or its use and function in the manner described and claimed herein:

Ultrasonic sprayers from Sonic and Materials, Inc., Misonix, Inc., Sono-Tek, Inc., Zevex International, Inc., U.S. Patents Nos. 3,765,606, 4,659,01, 5,104,042; 4,930,700, 4,153,201, 4,655,393, 5,516,043, 5,835,678, 5,879,364, and 5,843,139; etc., operate by passing liquid through a central orifice of an ultrasound instrument-tip, which creates problems with dosage control, heating of the drug, non-uniform particles, and other related difficulties.

Ultrasonic inhalers and drug delivery systems from Medisonic USA, Inc., 3M, Siemens Gmb, The Procter Gamble Company, Sheffield Pharmaceuticals, Aradigm, Inc., U.S. Patents Nos. 4,294,407, 5,347,998, 5,520,166, 5,960,792, 6,095,141, 6,102,298, 6,098,620, 6,026,808, and 6,106,547, operate by atomizing liquid using piezoceramic film and air/propellant.

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- U.S. Patent No. 4,912,357 describes a MHz oscillator with a concave surface adapted to the defined (limited V≤) liquid quantity to be atomized.
- In U.S. Patent No. 5,950,619 a propellant is used along with ultrasound. Another disadvantage of this device is that the atomization surface is button shaped, which creates uniform particles, and the distance between valve and atomization surface is hardly achievable in industrial assemble process (0.1 to 0.5 mm).
- U.S. Patents Nos. 5,586,550, 5,758,637, 5,938,117, 6,014,970, and 6,085,740 are based in driving liquid through the hole made on a piezofilm's working area. Bending waves are used, which spray non-uniform liquid particles.
- U.S. Patent No. 5,261,601 describes an atomizer having a membrane covering a liquid chamber. U.S. Patent No. 4,533,082 describes a liquid sprayer with multiple orifices on the vibrating element.

OBJECTS OF THE INVENTION

It is an object of the present invention to provide an improved device for oral pulmonary drug delivery.

It is also an object of the present invention to provide an improved device for oral pulmonary drug delivery using ultrasonic waves.

It is another object of the present invention to provide a device for the delivery of drugs ultrasonically with high efficiency.

It is yet another object of the present invention to provide a device for the delivery of drugs without the use of air or other propellants.

It is therefore an object of the present invention to provide a device for delivering drugs which affords highly precise dosage control.

It is a further object of the present invention to provide a method for the delivery of uniformed particles of a drug using ultrasonic waves.

These and other objects of the invention will become apparent from the following discussion below.

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SUMMARY OF THE INVENTION

The present invention provides for a drug delivery system. More particularly the present invention provides for a pocket size or hand held ultrasonic oral - pulmonary liquid and powder drug delivery device.

In one embodiment the device of present invention is characterized in that it is able to produce a spray and deliver it to the oral/pulmonary tract, without use of air or other propellants and with such spray having greater than about 90 % uniform particle size, with a high degree of dosage control.

The device of the invention comprises means for creating a directed spray of liquid or powder particles produced by contact of the liquid or powder with a radiation surface of ultrasound transducer such as, for example, a piezofilm/disk or ultrasound tip. The ultrasonic waves produced cause the spray to project outwardly from the radiation surface of the transducer. The particle spray is directed into the mouth for oral/pulmonary delivery.

According to the device of the present invention directed particle spray, created by ultrasound waves into a mouth delivers sharp dosage and uniform up to 90 % particle size drug.

Furthermore, the ultrasonic waves used in the device, energize the drug and cause penetration of the drug below the surface of the tissue.

Finally, the device of the invention for drug delivery is particularly advantageous when sharp dosage drug delivery is desirable, such as in insulin therapy for diabetic care, and similar applications.

The construction and obvious advantages of the system provided for by the present invention will be more clearly understood from the following description of the various specific embodiments when read in conjunction with the accompanying drawings.

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BRIEF DESCRIPTION OF THE DRAWINGS

- Fig. 1 is perspective view of the concept of an ultrasonic aerosol drug delivery device according to the present invention showing the principal elements as they relate to one another;
- Fig. 2 is a lateral cross-sectional elevational view of one embodiment of the ultrasonic aerosol drug delivery device according to the invention with a piezofilm or piezodisc working element;
- Fig. 3 is a lateral cross-sectional elevational view of another embodiment of the ultrasonic aerosol drug delivery device according to the invention, using an ultrasound tip with an enlarged distal end/radiation surface placed at an angle;
 - Fig. 4 is a lateral cross-sectional elevational view of another embodiment of the ultrasonic aerosol drug delivery device according to the invention, using an ultrasound tip with an enlarged distal end/radiation surface placed horizontally;
- Fig. 5 is a lateral cross-sectional elevational view of another embodiment of the ultrasonic aerosol drug delivery device according to the invention, using an ultrasound tip with a cylindrical distal end/radiation surface placed at an angle;
 - Fig. 6 is a lateral cross-sectional elevational view of another embodiment of ultrasonic aerosol drug delivery device according to the invention, using an ultrasound tip with the cylindrical end/radiation surface, placed horizontally;
 - Fig. 7 is a lateral cross-sectional elevational view of another embodiment of the ultrasonic aerosol drug delivery device according to the invention, using an ultrasound tip with a truncated angled distal end/radiation surface, placed horizontally; and
- Fig. 8 is a lateral cross-sectional elevational view of another embodiment of the ultrasonic aerosol drug delivery device according to the invention, using an alternative power supply as an AC adaptor.

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DETAILED DESCRIPTION OF THE INVENTION

The present invention is directed to a method and device of the present invention for ultrasonic aerosol drug delivery, characterized by a means for first delivering a liquid or powder drug to a radiation surface of an piezofilm/disk or ultrasonic transducer tip such that the liquid is dropped to the radiation surface under gravity. For this purpose, and to easily produce a spray, the radiation surface of the piezofilm/disk or ultrasonic transducer must be placed at some angle with relation to the horizontal. The actual radiation surface or geometric form of the ultrasound transducer tip may be one of many different shapes, such as, for example, cylindrical, oval, elliptical, square, rectangular, multi-angular, or another shape. Furthermore, the placement of the radiation surface at some angle allows one to get aerosol spray emanating from one point that is the touch point of the liquid with the radiation surface, which is a very important consideration and critical to obtaining uniform aerosol particle size. With the method and device of the present invention one is able to achieve substantial uniformity of particle size, to a degree of about 90 % or greater.

The step of producing the aerosol spray preferentially includes operating the transducer in such a manner as to produce ultrasonic waves having a frequency of from about 18 kHz to about 10,000 MHz. It is within the scope of the invention that the frequency could be less than about 18 kHZ or greater than 10,000 MHz.

The frequency may be constant, modulated or pulsed. The wave form produced may be sinusoidal, rectangular, trapezoid or triangular.

Frequencies below 18 kHz can be used as well; however, lower frequencies are less desirable due the fact that this range of sonic, or sound, waves can be uncomfortable to the patient. A most preferred range of frequencies is from about 20 to about 200 kHz. Frequencies of about 100 kHz are most preferred.

The device and method of the present invention can also include means for directing the spray into the mouth or at a target for from about 1 second to about 30 minutes, dependant upon the required dosage. The liquid or powder to be sprayed can

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include any drug, such as, for example, an antibiotic or antiseptic, and/or liquid which can be, for example, saline, water (distilled or regular), or oil.

The distance between the radiation surface of the transducer or piezofilm/disk and the liquid tube will preferably be about the size of liquid drop diameter ≈0.5 mm and above. Distances of less than 0.5 mm (up to 50 micron) can be used as well; however, this may cause some assembly difficulties.

In one preferred embodiment the method and device of present invention provides aerosol drug delivery with no air stream, no propellant and no pressure.

Fig. 1 depicts a basic concept of the ultrasonic aerosol drug delivery method and device according to the invention. A liquid (drug) drop or flow 10 falls under gravity to a radiation surface 13 of piezofilm/disk 15 via dispenser tube 12. Drop 10 contacts surface 13 at point 14 and creates directed aerosol 16. Radiation surface 13 of piezofilm/disk 15 is placed at an angle θ with respect to the horizontal.

In Fig. 2, which depicts a cross-sectional view of one preferred embodiment of the aerosol drug delivery device according to the invention, housing 24 includes piezofilm/disk 15 and liquid reservoir 19, which is may or may not be disposable. Housing 24 is also provided with a liquid dispenser 17, an electronic circuit board 20, a battery or capacitor 22, and an on/off button 21. Button 21 activates electronic circuit board 20, which is electrically connected to piezofilm/disk and causes piezofilm/disk 15 to oscillate. Liquid 18 from reservoir 19 is dispensed and delivered to radiation surface 13 (with an amplitude of ultrasound waves greater than 5 microns) at contact point 14, creating aerosol 16 which is directed to a mouth/target (not shown). Nozzle 25, which directs aerosol 16 into a patient's mouth/ target, may or may not be disposable.

Fig. 3 depicts a cross-sectional view of another embodiment of the aerosol drug delivery device according to the invention having an ultrasound transducer tip. The convenient location of surface 13 of a transducer tip 26 at an angle with the horizontal allows liquid or powder drop 10 delivered to the contact point 14 with gravity. The distance between distal end of tube 12 and contact point 14 or radiation surface 13 is less than or equal to the diameter of the liquid drop, and the aerosol drug delivery device

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will work in any position. If this distance between the distal end of tube 12 and contact point 14 on surface 13 is greater than a drop's diameter, then the device will only work vertically, which should not create a problem for the user.

Fig. 4 is a cross-sectional view of another preferred embodiment of the ultrasonic aerosol drug delivery device according to the invention with transducer tip 26. As illustrated, in this case liquid drop 10 must be directed exactly to the corner of the radiation surface of ultrasound tip 26. After touching the corner, liquid drop 10 pulls to the radiation surface 13, spreads and is aerosolized and directed to the mouth/target.

With reference to Figs. 5 and 6, which illustrate cross-sectional views of another preferred embodiment of the present invention, shown are a regular and cylindrical ultrasound transducer tip placed at an angle and horizontally, respectively.

With reference to Fig. 7, which illustrates a cross-sectional view of another embodiment according to the invention, shown are truncated cylindrical ultrasound tip 16, which allows one to create a liquid or powder aerosol spray more easily.

With reference to Fig. 8, which illustrates a cross-sectional view of another preferred embodiment according to the invention, shown are an ultrasonic aerosol drug delivery device with an alternative different power supply 23.

It will be further apparent to one skilled in this art that the improvements provided for in the present invention, while described with relation to certain specific physical embodiments also lend themselves to being applied in another physical arrangements not specifically provided for herein, which are nonetheless within the spirit and scope of the invention taught here.

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What is claimed is:

- 1. A device for ultrasonic drug delivery comprising:
- (a) means for producing oscillating ultrasonic waves, said means having a radiation surface;
- 5 (b) means for dispensing a liquid or powder onto the radiation surface, to produce an aerosol spray; and
 - (c) means for directing the said aerosol spray into a patient's mouth or onto another target.
- 2. The device according to Claim 1, wherein the means for producing the said oscillating ultrasonic waves comprises a piezofilm or disk, or a transducer tip.
 - 3. The device according to Claim 1, wherein the means for producing ultrasonic waves operates at a frequency of from about 18 kHz to about 10,000 MHz.
 - 4. The device according to Claim 1, wherein the means for producing ultrasonic waves operates at a frequency of from about 20 kHz to about 200 kHz.
- 15 5. The device according to Claim 1, wherein the means for producing ultrasonic waves operates at about 100 kHz.
 - 6. The device according to Claim 1, wherein the radiation surface is arranged within the device such that the radiation surface is maintained at a distance from the patient's mouth or the target to be treated.
- 7. The device according to Claim 1, wherein the radiation surface is positioned within the device at an angle with relation to the horizontal.
 - 8. The device according to Claim 7, wherein the radiation surface is positioned within the device at an angle with respect to the horizontal of from 0° to 90°.
 - 9. The device according to Claim 1, wherein the radiation surface is flat.
- 25 10. The device according to Claim 1, wherein the radiation surface is concave.

- 11. The device according to Claim 1, wherein the radiation surface is elliptic rounded.
 - 12. The device according to Claim 1, wherein the radiation surface is elliptic.
- 13. The device according to Claim 1, wherein the said radiation surface is oval.
 - 14. The device according to Claim 1, wherein the radiation surface is a combination of different geometrical forms.
 - 15. The device according to Claim 1, wherein the liquid or powder contacts the radiation surface such that an aerosol containing said liquid or drug is produced.
- 16. The device according to Claim 1, wherein liquid droplets contact the radiation surface at one point and are atomized.
 - 17. The device according to Claim 1, wherein liquid droplets spread on the radiation surface and are atomized.
- 18. The device according to Claim 1, wherein the means for producing ultrasonic waves operates at a fixed frequency.
 - 19. The device according to Claim 1, wherein the means for producing ultrasonic waves operates at a modulated frequency.
 - 20. The device according to Claim 1, wherein the means for producing ultrasonic waves operates at a pulsed frequency.
- 20 21. The device according to Claim 1, wherein the means for producing ultrasonic waves produces waves which are sinusoidal.
 - 22. The device according to Claim 1, wherein the means for producing ultrasonic waves produces waves which are rectangular.
- 23. The device according to Claim 1, wherein the means for producing25 ultrasonic waves produces waves which are trapezoidal.
 - 24. The device according to Claim 1, wherein the means for producing ultrasonic waves produces waves which are triangular.

- 25. A method for ultrasonic aerosol drug delivery comprising:
- (a) providing a means for producing oscillating ultrasonic waves, said means having a radiation surface;
- (b) providing a means for dispensing a liquid or powder onto the said
 radiation surface, in order to produce an aerosol spray;
 - (c) providing a means for directing the said aerosol spray into a patient's mouth or onto another target; and
 - (d) energizing the said means for producing the said ultrasonic waves.
- 26. A method for ultrasonic aerosol drug delivery comprising operating the device according to Claim 1.



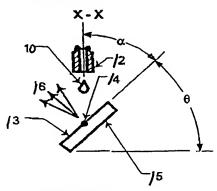


FIGURE 2

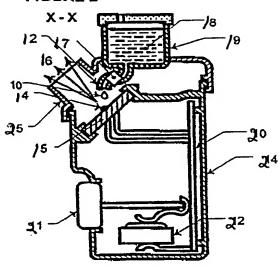
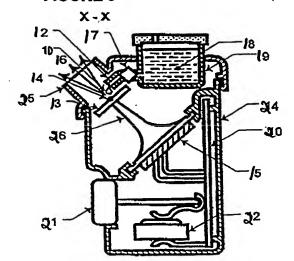


FIGURE 3



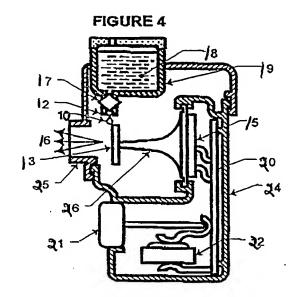


FIGURE 5

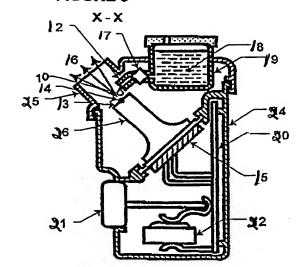
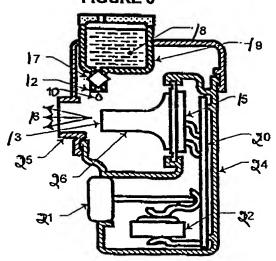
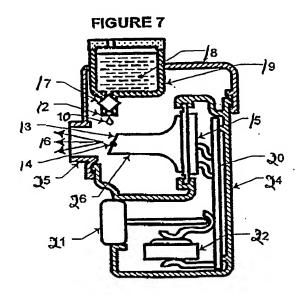
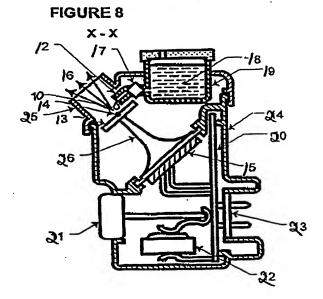


FIGURE 6







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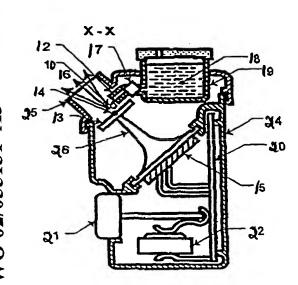
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(54) Title: METHOD AND DEVICE FOR ULTRASOUND DRUG DELIVERY



(57) Abstract: The present invention concerns a device for creating a directed spray (16) of liquid or powder particles (10) which is produced by contacting the liquid or powder (10) with a radiation surface (13) of an ultrasonic transducer such as a piezofilm or ultrasound tip (26). The ultrasonic waves cause the spray (16) to project outwardly from the radiation surface (13) and directs it into a patient's mouth or onto another target. Directed particle spray (16) delivers sharp dosage and uniformed up to 90 % particle size drug delivery.

INTERNATIONAL SEARCH REPORT

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INTERNATIONAL SEARCH REPORT

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